

### REMARKS

Upon entry of the present amendment, claims 1-14, 16, 20, 25-36, 38-50, and 52-57 will be pending. Claims 10, 14, 26-36, 38-50, and 52-57 are withdrawn. Claims 15, 17-19, 21-24, 37, and 51 have been canceled without prejudice. Applicants have amended claims 1, 3, 4, 34, 55, and 56 to more clearly point out the claimed subject matter. Support for the amendments can be found throughout the specification, for example, at page 5, line 18; page 13, lines 17-19; page 26, lines 1-3; and page 27, lines 23-25; and Example 1. No new matter has been introduced.

#### Withdrawn objections and rejections

Applicants note with appreciation that the Office has withdrawn the objection to the specification and a number of rejections under 35 U.S.C. § 103.

#### 35 U.S.C. § 103

The Office rejected claims 1, 2, 5, 11, 12, 16, 20, and 25 as allegedly obvious over Webb et al. (WO 97/46256; "Webb") in view of Rhode et al. (U.S. Patent No. 6,232,445; "Rhode"), Lehmann et al. (U.S. Patent No. 5,939,281; "Lehmann"), and Wagner et al. (U.S. Patent No. 6,329,209; "Wagner").

According to the Office Action mailed July 22, 2008 ("the Office Action"):

... Webb et al. is silent on disclosing that the each group of spatially distinct areas comprises a plurality of different MHC-peptide complexes ... Webb et al. further fails to teach that the substrate is flat ... Rhode et al. further teaches that an array of MHC complexes can be formed on a substrate such as 96-well plates ... Lehmann et al. teaches a method of detecting secreted cytokines by activated T-cells using cytokine capture assay ... because Wagner et al. teaches that substrate of an array having both flat and non-flat features (such as wells) can be used to provide support for the protein arrays, it would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the multi-well plate format of Webb et al. in view of Rhode et al. and Lehmann et al. for the flat substrate format of Wagner et al. to achieve to predictable result of providing a suitable support for the protein array.

Applicants respectfully traverse with respect to the presently amended claims.

As an initial matter, applicants disagree with the Office's assertion (at pages 9-10 of the Office Action) that the recitation of "spatially-distinct areas are configured to allow contact with one sample at essentially the same time and with the same sample" provides no patentability weight. However, to expedite prosecution of this application, applicants have amended claim 1 to recite an array comprising a flat substrate and a plurality of MHC molecules complexed with antigen-derived peptides immobilized in spatially-distinct areas on the substrate. The array further includes at least one hydrophobic barrier that surrounds a plurality of the spatially-distinct areas, and each area in the plurality of the spatially-distinct areas is not surrounded individually by a separate hydrophobic barrier, such that when a single volume of sample is applied inside of the single hydrophobic barrier, all areas in the plurality of said spatially-distinct areas are in contact with the single volume of sample. As one of skill in the art will appreciate, an array so configured would allow fluid communication between all of the plurality of spatially-distinct areas inside the single hydrophobic barrier.

As acknowledged in the Office Action (at page 6), Webb discloses immobilizing MHC class II molecules to wells of microtiter plates. The Office appears to equate each well to a "spatially distinct area" as recited in claim 1 (see Office Action at page 6). Even so construed, skilled practitioners would appreciate that each well of a microtiter plate is separated from each other structurally such that there can be no fluid communication between the wells of a microtiter plate. Thus, Webb fails to suggest the claimed array.

Rhode fails to rectify the deficiencies of Webb. Like Webb, Rhode discloses using 96-well microtiter plates (as noted in the Office Action at page 7).

Neither does Lehmann remedy these deficiencies. Lehmann also discloses using microtiter plates (see, e.g., column 6, lines 15-17; and column 21, lines 17-20), and does not provide any additional information that would have led skilled practitioners to applicants' claimed array.

Wagner also fails to remedy these deficiencies. The reference describes an array with a substrate and a plurality of discrete "patches" that each includes protein-capture agents immobilized on the substrate. Even if one were to construe the "patch" of Wagner as equivalent

to a "spatially distinct area" recited in the present claims, Wagner does not disclose or suggest the claimed array. Example 1 of Wagner (see, e.g., column 38, lines 39-45) describes an array with patches that are individually surrounded and separated from each other by hydrophobic surface areas. Wagner further discloses in Example 2 (see, e.g., column 39, lines 1-6) making an array by coating a wafer entirely with a hydrophobic layer before placing the patches onto the wafer. As such, one of skilled in the art would reasonably concluded that the patches on the array described in Example 2 are each surrounded by hydrophobic areas. Moreover, all of the claims in Wagner recite an array device having "an array of spaced-apart immobilization regions ... ,said immobilization region having therein a plurality of protein-capture agents ... [and] one or more border regions surrounding each immobilization region and separating such immobilization regions from one another, said border region each comprising (i) an ordered hydrophobic monolayer ... (emphasis added)" In other words, Wagner describes arrays with patches that are individually surrounded by and separated from each other by hydrophobic borders. Thus, Wagner does not describe or suggest the claimed array that has a plurality of spatially-distinct areas surrounded by a single hydrophobic barrier, wherein each spatially-distinct areas is not surrounded individually by a separate hydrophobic barrier, such that when a single volume of sample is applied inside of the single hydrophobic barrier, all areas in the plurality of said spatially-distinct areas are in contact with the single volume of sample.

Accordingly, Webb, Rhode, Lehmann and Wagner, individually or combined, do not teach or suggest every element of the claims. Since no combination of these references suggests applicants' claimed array, these references would not have led those skilled in the art to the claimed array. The Office, therefore, has failed to establish a *prima facie* case of obviousness.

Even assuming that a *prima facie* case of obviousness could be established (which applicants explicitly do NOT concede), applicants previously presented surprising results sufficient to overcome such a case (see, e.g., applicants' AMENDMENT IN REPLY TO ACTION OF APRIL 9, 2007, and AMENDMENT IN REPLY TO ACTION OF DECEMBER 27, 2007). As applicants discussed at length in their previous submissions, one of skill in the art at the time of the invention would not have expected that applicants' array would work. The

present Office Action does not appear to address applicants' evidence of surprising results, which is equally applicable to the present rejections. Applicants respectfully note that, according to MPEP § 2145, "[evidence] pertaining to secondary considerations must be taken into account whenever present ... If the evidence is deemed insufficient to rebut the *prima facie* case of obviousness, Office personnel should specifically set forth the facts and reasoning that justify this conclusion."

In view of the foregoing, applicants submit that the present claims are not obvious over any combination of Webb, Rhode, Lehmann and Wagner. Reconsideration and withdrawal of this rejection are respectfully requested.

The Office also rejected claims 3, 4, 6, and 7 as allegedly obvious over Webb, Rhode, Lehmann, Wagner, and Taylor (U.S. Patent No. 6,103,479). Applicants respectfully traverse for at least the reasons stated below.

Claims 3, 4, 6 and 7 depend from claim 1, and therefore, are not obvious over Webb, Rhode, Lehmann and Wagner for at least the reasons set forth above. Taylor fails to remedy the deficiencies of these four references. In fact, as pointed out in applicants' previous reply (see pages 17-18 of AMENDMENT IN REPLY TO ACTION OF DECEMBER 27, 2007), Taylor teaches away from applicants' claimed array. Taylor describes a non-uniform micro-patterned array with hydrophilic spots that Taylor refers to as "wells" (see, e.g., column 8, lines 35-37). As shown in FIGs. 1A and 1B of Taylor, for example, each "well" is surrounded by a hydrophobic material that isolates each "well" from all other "wells." Taylor also describes a microfluidic delivery system that has a multitude of individual microfluidic channels, each of which delivers fluid to an individual well (see, e.g., column 13, line 57 to column 14, line 43; and Figs. 4, 5 and 10). As described in Example 2 of Taylor, such a microfluidic delivery system was used to deliver an array of compounds to an array of wells each containing cells, to determine which compound induced a specific response in these cells. That is, the wells in Taylor's array are divided from each other by separate barriers, and designed to receive separate samples, rather than be in contact simultaneously with one single sample.

Accordingly, skilled practitioners would have had reasonably concluded that the array described in Taylor is more like a microtiter plate, in which each well is a separate assay chamber. Those skilled in the art would not have gleaned from Taylor any reason to arrive at applicants' claimed array. Moreover, as Taylor's array is designed to include wells that are separated from each other, Taylor would have led a skilled practitioner away from applicants' array, which has a plurality of spatially-distinct areas within a single hydrophobic barrier, wherein each area is not surrounded by its own barrier, to be in contact simultaneously with a single volume of sample.

In view of the foregoing, Webb, Rhode, Lehmann, and Taylor, either singly or in combination, fail to disclose or suggest the claimed array, and Taylor teaches away from the array. Applicants submit that the present claims are not obvious in view of these references, and respectfully request withdrawal and reconsideration of this rejection.

The Office also rejected claims 8 and 9 as allegedly obvious over Webb in view of Rhode, Lehmann, Wagner, and Tom-Moy et al. (U.S. Patent No. 6,235,488; "Tom-Moy"). Applicants respectfully traverse.

The deficiencies of Webb, Rhode, Lehmann and Wagner are as set forth above. Tom-Moy also does not suggest the claimed array. The Office Action (at page 14) cites Tom-Moy only for disclosing the substitution of streptavidin for avidin, and Tom-Moy fails to provide any other relevant information to remedy the deficiencies of Webb, Rhode, Lehmann and Wagner. Accordingly, claims 8 and 9 are not obvious over these references, individually or combined. Applicants respectfully request withdrawal of this rejection.

Finally, the Office rejected claim 13 as allegedly obvious over Webb in view of Rhode, Lehmann, Wagner, Abraham et al. (J. Immunol., 20014, Vol. 167, pp5193-5201; "Abraham") and Mikesell et al. (U.S. Pub. No. US 2002/0095024; "Mikesell"). Applicants respectfully traverse.

The deficiencies of Webb, Rhode and Lehmann are as discussed above. The Office Action (at page 15) cites Abraham and Mikesell for disclosing the use of anti-CD11a antibodies as costimulatory antibodies. These references do not suggest applicants' array and, therefore, fail to rectify the deficiencies of Webb, Rhode and Lehmann. Thus, claim 13 is not obvious over these references, individually or in combination. Reconsideration and withdrawal of this rejection are respectfully requested.

#### CONCLUSION

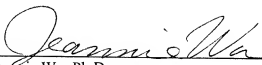
Applicants respectfully request that all claims be allowed. Applicants do not concede any positions of the Examiner that are not expressed above, nor do applicants concede that there are not other good reasons for patentability of the presented claims or other claims.

The extension fee in the amount of \$555 is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 07917-0212001.

Respectfully submitted,

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